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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
TSAY, MARSHA M	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/566,354	SCHULZ ET AL.	
	Examiner	Art Unit	
	Marsha M. Tsay	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 20, 2008, has been entered.

Applicants' arguments have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous Office actions are hereby withdrawn.

Claims 1-20 are pending and currently under examination.

Priority: The request for priority to provisional application 60/494097, filed August 12, 2003, is acknowledged.

Objections and Rejections

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 12 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 12 has currently been amended to include the limitation, wherein the plasma-like form of A1AT has a maximum activity of 100%. Applicants assert that one of skill in the art knows that the A1AT activity of natural is 100%. Applicants point to Mattes et al. for support. For example, Mattes et al. disclose that an active-inactive ratio of A1AT of at least 120% is greater than the ratio found in plasma (see abstract). Further, Mattes et al. state that the "relative plasma A1AT activity is defined as the ratio of active to inactive A1AT, this ratio in plasma being assumed to be 100% or relative plasma A1A% activity." (Mattes et al. p. 6). Thus, one of ordinary skill would know that natural plasma has an A1AT activity of 100%.

This is not found convincing because while Mattes et al. do provide support for relative plasma A1AT activity, which is defined as the ratio of active to inactive A1AT, it should be noted that instant claim 12 recites A1AT in its "plasma-like form" and that the "plasma-like form" of A1AT has a maximum activity of 100%. Based on Mattes et al., one of ordinary skill would know that A1AT has a relative plasma activity. However, it would be unclear to one of ordinary skill what is meant by "plasma-like" form. Further, there does not appear to be any support for "plasma-like form" in the instant specification or a definition of what is meant by "plasma-like."

Also, as previously noted, it is unclear how one of ordinary skill would find it apparent that the maximal activity of A1AT is 100% based on a SDS-PAGE indicating that A1AT has a MW of 50 kD. It is known in the art that in plasma, A1AT has an active and an inactive isomer (Mattes et al.). Based on Mattes et al., one of ordinary skill would know that the plasma A1AT activity is related and/or determined by the amount of inactive A1AT present in a preparation. Since it is still unclear how Applicants determined the instant maximum activity of A1AT (i.e.

100%), (since there is no reference to the amount of inactive A1AT present in the instant claims or the specification), instant claim 12 is still believed to contain new matter.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 9-11, 13-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a process for purifying A1AT at concentrations and conditions including 0.1% (w/w) Triton and Tween 80, 0.03% (w/w) tri-n-butyl phosphate, 0.1 mM caprylic or caprylate, an incubation time of 0.1 hours (claim 4), a salt concentration of 0.5 M (claim 5), pasteurization in the presence of 0.5 M sodium citrate (claim 8), an incubation temperature at 15°C (claim 13e), does not reasonably provide enablement for said process at concentrations and conditions including >0.1% (w/w) Triton and Tween 80, >0.03% (w/w) tri-n-butyl phosphate, >0.1 mM caprylic or caprylate, an incubation time of >0.1 hours (claim 4), a salt concentration of >0.5 M (claim 5), pasteurization in the presence of >0.5 M sodium citrate (claim 8), an incubation temperature at >15°C (claim 13e). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The scope of the instant claims is not commensurate with the enablement of the instant disclosure, because practice of the claimed invention would require undue experimentation by an artisan of ordinary skill in the art to ascertain which concentrations, incubation time, and temperatures greater than the values noted above will allow a functionally active A1AT to be

purified. Thus for the instant claimed invention, it would require an undue burden of experimentation for a skilled artisan to determine exactly which values above >0.1% (w/w) Triton and Tween 80, >0.03% (w/w) tri-n-butyl phosphate, >0.1 mM caprylic or caprylate, an incubation time of >0.1 hours (claim 4), a salt concentration of >0.5 M (claim 5), pasteurization in the presence of >0.5 M sodium citrate (claim 8), an incubation temperature at >15°C (claim 13e) will allow the purification of an A1AT having a purity >90% and an activity of ≥0.8 PEG/mg.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

In the instant case the quantity of experimentation would be large since any value >0.1% (w/w) Triton and Tween 80, >0.03% (w/w) tri-n-butyl phosphate, >0.1 mM caprylic or caprylate, an incubation time of >0.1 hours (claim 4), a salt concentration of >0.5 M (claim 5), pasteurization in the presence of >0.5 M sodium citrate (claim 8), an incubation temperature at >15°C (claim 13e) can be chosen. The amount of guidance is minimal with regard to which values above the base conditions will result in the purification of a functional A1AT having a purity >90% and an activity of ≥0.8 PEG/mg. In Example 1 of the specification (p. 11-12), Applicants disclose a solvent/detergent treatment comprising using 1% (w/w)Triton X-100, 0.3% (w/w) tri-n-butyl phosphate, for 4 hours at 20°C, and a salt concentration of 1.5M sodium citrate. The nature of the invention is such that a change in the concentration of the salt solution, detergents, incubation period, and/or temperature may disrupt the structure and therefore, the activity of the protein (A1AT). The state of the prior art is that proteins are sensitive to their environment and any changes to their physical environment may disrupt their activity. The relative level of skill in this art is very high. The predictability as to which values >0.1% (w/w) Triton and Tween 80, >0.03% (w/w) tri-n-butyl phosphate, >0.1 mM caprylic or caprylate, an incubation time of >0.1 hours (claim 4), a salt concentration of >0.5 M (claim 5), pasteurization in the presence of >0.5 M sodium citrate (claim 8), an incubation temperature at >15°C (claim 13e) will confer a functional A1AT having a purity >90% and an activity of ≥0.8 PEG/mg is zero.

When the factors are considered in their entirety, the Wands analysis dictates a finding of undue experimentation and thus, the claim is not enabled.

In their remarks, Applicants assert that the specification provides a working example of the claimed process in Example 1. The specification further describes the methods, including reagents used, and the desired results of some embodiments of the claimed process in paragraphs [0019], [0021], and [0026]-[0033]. Applicants assert that when the specification as a whole is considered, one of skill in the art would be able to make or use the claimed invention without undue experimentation. Applicant's arguments have been fully considered but they are not persuasive.

It should first be noted that the instant 35 U.S.C. 112, first paragraph, rejection is a scope of enablement rejection; therefore, the working example noted by Applicants in their remarks was previously and instantly noted to be enabled. While the instant specification is enabled for the process of purifying A1AT at concentrations and conditions including 0.1% (w/w) Triton and Tween 80, 0.03% (w/w) tri-n-butyl phosphate, 0.1 mM caprylic or caprylate, an incubation time of 0.1 hours (claim 4), a salt concentration of 0.5 M (claim 5), pasteurization in the presence of 0.5 M sodium citrate (claim 8), an incubation temperature at 15°C (claim 13e), it does not reasonably provide enablement for said process at concentrations and conditions including >0.1% (w/w) Triton and Tween 80, >0.03% (w/w) tri-n-butyl phosphate, >0.1 mM caprylic or caprylate, an incubation time of >0.1 hours (claim 4), a salt concentration of >0.5 M (claim 5), pasteurization in the presence of >0.5 M sodium citrate (claim 8), an incubation temperature at >15°C (claim 13e). As the claims are currently written, there are no upper limits to the concentration of Triton (>0.1%) or Tween 80 (0.03%) used or to the incubation time (>0.1 hours) used in said process for purifying A1AT, for example. Therefore, any value above the base values recited in the instant claims is encompassed by the instant process as recited in the

claims. However, the specification does not provide appear to have support for all values above the base values, except for the values noted above and in the working example. Therefore, it would be undue experimentation to determine which values >0.1% (w/w) Triton and Tween 80, >0.03% (w/w) tri-n-butyl phosphate, >0.1 mM caprylic or caprylate, an incubation time of >0.1 hours (claim 4), a salt concentration of >0.5 M (claim 5), pasteurization in the presence of >0.5 M sodium citrate (claim 8), an incubation temperature at >15°C (claim 13e) will confer a functional A1AT having a purity >90% and an activity of ≥0.8 PEG/mg.

For at least these reasons, the 35 U.S.C. 112, first paragraph, scope of enablement rejection is enabled.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 12-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12 recites alpha-1-antitrypsin is in its "plasma-like form." It is unclear what is meant by "plasma-like" form. The specification does not appear to have a definition for "plasma-like".

Claims 13-20 are included in this rejection because they are dependent on the above claims and fail to cure the defect.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 12-18, 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Mattes et al. (AU 199874180 B2; IDS as WO9856821; previously cited). Claims 12-19 are drawn to an A1AT protein composition. Mattes et al. teach a purified A1AT protein product (p. 24 Table 2). The purified A1AT product obtained by the method of Example 2 has a purity of >90% (~118%) and has a specific activity of ≥0.8 PEU/mg (~1.0 PEU/mg) (p. 24; claims 12-18, 20). Mattes et al. also teach the A1AT composition can be prepared as a solution or a lyophilized preparation as well as a method of preparing such a composition (p. 26 claim 11; claims 17-18).

While Mattes et al. do not explicitly teach the elements of an IgA content ≤1 mg/mL, a residual detergent of <50 ppm, or a monomer content of >90%, these elements are believed to be anticipated by Mattes et al. since the A1AT protein product of Mattes et al. already meets the instant elements of having a purity >90% (~118%), it would inherently not contain additional protein components or residual detergents, and since it has a specific activity of ≥0.8 PEU/mg (~1.0 PEU/mg), it would inherently have a monomer content of >90%. Instant claims 13-17 are dependent on the A1AT product of claim 12 and recite the process on how it is obtained. However, the method steps recited in claims 13-17 do not change the A1AT protein product, i.e. they are still drawn to an A1AT protein having a purity of >90% and a specific activity of ≥0.8 PEU/mg. Since Mattes et al. teach an A1AT protein product that meets the limitations of claim

12, claims 13-17 are also anticipated by Mattes et al. because they are drawn to the same product.

In their remarks, Applicants assert that claim 12 has been amended to recite that the "the plasma-like form of A1AT has a maximum activity of 100%." In contrast, Mattes et al. disclose a method of preparation with A1AT having an activity of at least 120%, which is greater than that in plasma. This increased activity results from a greater ratio of active to inactive A1AT in the preparation than is present in plasma (abstract Mattes et al.). Applicant's arguments have been fully considered but they are not persuasive.

Firstly, as noted in the 35 U.S.C. 112, 2nd paragraph, rejection above, it is unclear what is meant by "plasma-like form." Therefore, claim 12 is essentially drawn to an A1AT having a purity of >90%, an activity of ≥0.8 PEU/mg, etc., and having a maximum activity of 100%.

Applicants point to Mattes et al. to note that one of ordinary skill would know that A1AT in plasma has a maximum activity of 100%, since Mattes et al. disclose that a greater ratio of active to inactive A1AT of results in A1AT having a greater activity than found in plasma, i.e. 120%. This is also noted in Mattes et al. p. 6, paragraph 3. Therefore, the A1AT preparation of Mattes et al. appears to have a higher concentration of active A1AT compared to inactive A1AT (p. 9), such that it has a relative plasma A1AT activity of at least 120% and that its portion of inactive A1AT is less than 10% (p, 6 third paragraph). Therefore, one of ordinary skill would know that the plasma A1AT activity is related and/or determined by the amount of inactive A1AT present in a preparation. Since it is still unclear how Applicants determined the instant maximum activity of A1AT (i.e. 100%), (since there is no reference to the amount of inactive

A1AT present in the instant claims or the specification), the instant claims remain rejected under Mattes et al. because Mattes et al. teach a A1AT protein having a purity >90% (~118%), which would inherently not contain additional protein components or residual detergents, and a specific activity ≥0.8 PEU/mg (~1.0 PEU/mg), which would therefore, inherently have a monomer content of >90%.

For at least these reasons, the Mattes et al. reference is maintained.

Claims 1-5, 9-11 remain rejected under 35 U.S.C. 102(b) as being anticipated by Taniguchi et al. (US 6284874; previously cited). Taniguchi et al. teach a method of purifying alpha-1 proteinase inhibitor, also known as α_1-antitrypsin (A1AT), by flow-through chromatography, viral inactivation, and filtration (col. 2-4). In Example 1, Taniguchi et al. teach a plasma fraction of IV_1+IV_4 was solubilized in PEG/$ZnCl_2$, applied to a QAE anionic-exchange chromatographic column (col. 6 lines 60-65; claim 1a), eluted, and diafiltered (col. 7 lines 1-10). Taniguchi et al. further teach that 1.1 kg of a detergent solution of 10% w/v polysorbital 80 and 3% w/v tri-n-butyl phosphate (TnBP) was added to the diafiltered A1AT and incubated at 25°C for 1 hr. to inactivate any viral contaminants (col. 7 lines 10-15; claim 1b). The A1AT solution was then applied to a copper chelating medium and washed with 150 mM NaCl, 500 mM NaCl (col. 7 lines 20-25; claim 1c). The A1AT solution was the ultrafiltered, filtrate was collected, and diafiltered by ultrafiltration against 50 mM NaCl (col. 7 lines 30-35; claim 5, 9). Taniguchi et al. teach the filter used has a 100 kD MWCO, which is in the range of a filter having a pore size between 15-20 nm (col. 5 line 31-32; claim 10).

In their remarks, Applicants assert claim 1 has been amended to clarify the order of the steps in the claimed method. The claimed method of purifying involves salting the detergents out after treatment (e.g. applying the salt to the elution of the ion-exchange chromatography), as disclosed in instant Example 1. In contrast, Taniguchi et al. disclose the addition of a detergent (polysorbital 80) which is followed by cooling the solution, adjusting the pH, applying the solution to a copper chelating medium and then washing the resulting medium with NaCl solution. This reference does not disclose a salting step directly after the addition of a detergent as amended claim 1 requires. Applicant's arguments have been fully considered but they are not persuasive.

Claims 1-5, 9-11 are drawn to a process for purifying A1AT from A1AT solutions comprising the steps as recited in the claims. As previously noted, the use of open language "comprising" allows for the inclusion of other unspecified steps and/or ingredients in the claim interpretation. Therefore, while Taniguchi et al. may teach the additional steps as noted in Applicants' remarks, Taniguchi et al. still teach claim steps 1(a), 1(b), and 1(c), as noted above, which includes adding NaCl (increasing the salt concentration) to the A1AT solution after ion-exchange chromatography (claim 1(c)). Even if Taniguchi et al. do not explicitly state that adding NaCl will salt out the detergents, the "salting out" process would inherently occur since the salt concentration of the A1AT solution was increased by adding NaCl solution.

For at least these reasons, the Taniguchi et al. reference is maintained.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Taniguchi et al. (US 6284874) in view of Isaksson et al. (WO 9426287; IDS). The teachings of Taniguchi et al. are outlined above. Taniguchi et al. do not teach a heparin gel or a pasteurization step.

Isaksson et al. teach a process for reduction of virus inactivating chemicals and/or detergents in an aqueous composition containing a water-soluble plasma protein (abstract). Isaksson et al. further teach that when the aqueous base comprises a salt of citrate at >1 M, the virus inactivating chemical or detergent can give a final concentration below 5 ppm (abstract). Isaksson et al. teach the method is applicable to any plasma protein (p. 6 lines 15-20). In example I, Isaksson et al. teach the plasma protein antithrombin III (AT III) was separated from plasma by using a heparin sepharose gel (p. 7 lines 15-18). Isaksson et al. further teach an additional virus inactivation step of incubating the plasma protein solution in 2 M sodium citrate (p. 7 lines 20-30).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Taniguchi et al. by substituting the heparin sepharose gel of Isaksson et al. for the anionic-exchange column used in Taniguchi et al. (claims 6-7). One of ordinary skill would recognize that the chromatographic step can be substituted with a functionally equivalent column that is commercially available and would expect to have a reasonable level of success in using a heparin sepharose gel to isolate A1AT because Isaksson et al. disclose its success application in separating another plasma protein.

It would also have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Taniguchi et al. by including the additional virus inactivation step of Isaksson et al. to the A1AT purification process of Taniguchi et al. (claim 8). The motivation to do so is given by Isaksson et al. which disclose that sodium citrate helps in reducing the residual detergent content and therefore, would result in a purer protein product.

In their remarks, Applicants assert that Taniguchi et al. does not discuss "salting out" of the detergents according to the instant claims.

The Taniguchi et al. reference is relevant art and is maintained for the reasons noted above.

Applicants further assert that Isaksson et al. disclose the removal of detergents using a sodium citrate method but its final product is medically unacceptable because, as seen in Example 4, it comprises 250 ppm Triton X-100 and 35 ppm TnBP. Applicant's arguments have been fully considered but they are not persuasive.

The reasons are the same as previously noted, but are summarized herein. The Isaksson et al. reference was used to remedy the Taniguchi et al. reference because the Taniguchi et al. reference does not teach a virus inactivation step. Isaksson et al. disclose that the virus inactivation step can be applied, in general, to water-soluble plasma proteins, i.e. factor VIII, factor IX, albumin, alpha1-acid glycoprotein. It is known in the art that A1AT is a plasma protein (Mattes et al.). In Examples 1-4, Isaksson et al. disclose non-limiting examples of applying a virus inactivation step to proteins (antithrombin III, transferring, albumin) isolated/purified by different processes (p. 7-9). In Example 1, the AT III is separated from

plasma by Heparin Sepharose gel; in example 2, the transferring is isolated in "Cohn's cold ethanol method" followed by chromatography; in example 3, the AT III is isolated by sepharose gel; and in example 4, the albumin is isolated by a modified "Cohn's cold ethanol method." Applicants assert that Isaksson et al. disclose the removal of detergents using a sodium citrate method but its final product is medically unacceptable because, as seen in Example 4, it comprises 250 ppm Triton X-100 and 35 ppm TnBP. One of ordinary skill would recognize that the higher detergent concentration in example 4 is due to the lack of an additional chromatographic step, and not the virus inactivation step (see Example 2 vs. Example 4). Therefore, depending on the isolation/purification process used to purify the plasma protein, one of ordinary skill would recognize that the virus inactivation step of Isaksson et al. would only help in reducing residual detergent content and result in a purer protein product.

Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Mattes et al. (AU 199874180 B2; IDS as WO9856821). Mattes et al. disclose A1AT deficiencies include degenerative lung disease, i.e. emphysema (p. 4). As noted above, Mattes et al. disclose an A1AT protein having a purity of >90% and a specific activity of $\geq$0.8 PEU/mg. Mattes et al. do not explicitly teach a method of treating a degenerative lung phenomena of the lung comprising administering A1AT to a subject in need thereof.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to administer the A1AT of Mattes et al. to a subject for treating a degenerative lung disease because Mattes et al. disclose A1AT deficiency is associated with degenerative lung disease and it would be reasonable for one of ordinary skill to expect that administering an

A1AT protein having a purity of >90% and a specific activity of ≥0.8 PEU/mg would be successful in overcoming the A1AT deficiency since their is a direct correlation between plasma level of functional A1AT to lung disease (claim 19).

In their remarks, Applicants assert Mattes et al. do not disclose or teach the claimed A1AT having the "plasma-like" activity as set forth in claim 12, from which claim 19 depends. Applicant's arguments have been fully considered but they are not persuasive.

Due to the indefiniteness issue of "plasma-like" as noted above, the Mattes et al. reference is still believed to be relevant art for the same reasons as noted above.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marsha M. Tsay whose telephone number is (571)272-2938. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Maryam Monshipouri/

Primary Examiner, Art Unit 1656

November 3, 2008